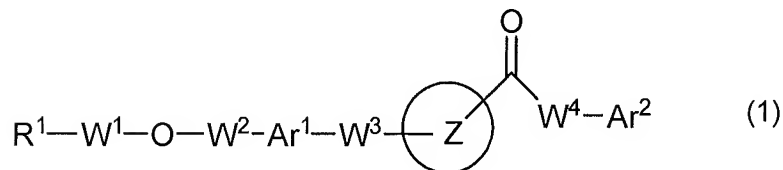


**AMENDMENTS TO THE CLAIMS**

1. – 17.(Canceled)

18. (New) A heteroaryl derivative of the formula (1):



or a pharmaceutically acceptable salt thereof,

wherein R¹ is a carboxyl group;

W¹ and W² are an optionally substituted lower alkylene;

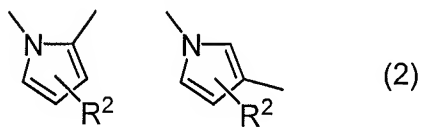
Ar¹ is an optionally substituted phenylene, an optionally substituted pyridine-diyl, or an optionally substituted thiophene-diyl;

W³ is a lower alkenylene;

W⁴ is a single bond;

Ar² is an optionally substituted phenyl;

Ring Z is selected from the following formulae (2):



in which the number of R² may be one or more, and each is independently selected from a hydrogen atom, a halogen atom, an optionally substituted alkyl, an optionally substituted aryl, an optionally substituted heteroaryl, and an optionally substituted thiol, and either of the binding direction of these groups may be acceptable;

wherein the heteroaryl is a heteromonocyclic aryl or heterobicyclic aryl having 1 to 3 heteroatoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, which is a 5-membered monocyclic heteroaryl, a 6-membered monocyclic heteroaryl or a bicyclic heteroaryl;

the optionally substituted aryl, the optionally substituted heteroaryl, the optionally substituted phenylene, the optionally substituted pyridine-diyl and the optionally substituted

thiophene-diyl may have 1 to 5 substituents at any substitution available position, said substituent being a member selected from an optionally substituted lower alkyl, a lower alkenyl, an aryl, a substituted aryl, a heteroaryl, a substituted heteroaryl, an optionally substituted non-aromatic heterocyclic group, a halogen atom, an optionally substituted amino, an optionally substituted acyl, an optionally substituted hydroxy, an optionally substituted thiol, an alkylsulfonyl, cyano, nitro, and a carbamoyl group optionally substituted by an alkyl;

the lower alkyl of the optionally substituted lower alkyl is a straight chain or branched chain C<sub>1</sub>-C<sub>8</sub> alkyl, or a C<sub>1</sub>-C<sub>8</sub> alkyl having a cyclic structure, the substituent of said optionally substituted lower alkyl being a member selected from hydroxy, oxo, amino, a C<sub>1</sub>-C<sub>8</sub> monoalkylamino, a C<sub>2</sub>-C<sub>12</sub> dialkylamino, a C<sub>1</sub>-C<sub>8</sub> alkoxy, a halogen atom, a C<sub>1</sub>-C<sub>8</sub> haloalkoxy, a non-aromatic heterocyclic group, an aryl, and a heteroaryl;

the lower alkenyl is a straight chain or branched chain C<sub>2</sub>-C<sub>8</sub> alkenyl or a C<sub>2</sub>-C<sub>8</sub> alkenyl having a cyclic structure;

the aryl is phenyl, 1-naphthyl, or 2-naphthyl;

the non-aromatic heterocyclic group is one having as the ring-forming atoms 2 to 6 carbon atoms and 1 to 3 heteroatoms selected from an oxygen atom, a sulfur atom and a nitrogen atom in addition to the carbon atoms;

the substituent of said substituted aryl, substituted heteroaryl, optionally substituted non-aromatic heterocyclic group is a member selected from a C<sub>1</sub>-C<sub>8</sub> alkyl, a C<sub>1</sub>-C<sub>8</sub> alkoxy, a halogen atom, and a C<sub>1</sub>-C<sub>8</sub> haloalkoxy;

the optionally substituted amino is amino, or an amino optionally substituted by one or two groups selected from a C<sub>1</sub>-C<sub>8</sub> alkyl, a C<sub>1</sub>-C<sub>8</sub> acyl, an aryl, and a heteroaryl;

the acyl is formyl, a group combining a carbonyl group and a C<sub>1</sub>-C<sub>8</sub> alkyl, an aryl, or a heteroaryl, said acyl group having optionally 1 to 3 substituents at any substitution possible position, which are a member selected from a straight chain or branched chain C<sub>1</sub>-C<sub>3</sub> alkyl, a straight chain or branched chain C<sub>1</sub>-C<sub>3</sub> alkoxy, a halogen atom, hydroxy, and amino;

the optionally substituted hydroxy group is a hydroxy, an optionally substituted alkoxy, an optionally substituted aralkyloxy, an optionally substituted aryloxy, or an optionally substituted acyloxy;

the alkoxy of the optionally substituted alkoxy is a C<sub>1</sub>-C<sub>8</sub> alkoxy, and when an alkyl or an alkoxy exists adjacently, then said group may combine together with an adjacent group to form a ring having a substituent;

the aralkyloxy of the optionally substituted aralkyloxy is a phenyl-(C<sub>1</sub>-C<sub>4</sub>alkyl)oxy;

the aryloxy of the optionally substituted aryloxy is phenyloxy, or 1-naphthyloxy;

the acyloxy of the optionally substituted acyloxy is acetyloxy or propionyloxy;

the substituent of the above-mentioned optionally substituted alkoxy, optionally substituted aralkyloxy, optionally substituted aryloxy, or optionally substituted acyloxy is a member selected from a halogen atom, a straight chain or branched chain C<sub>1</sub>-C<sub>3</sub> alkoxy, a straight chain or branched chain C<sub>1</sub>-C<sub>3</sub> alkyl, trifluoromethyl, and trifluoromethoxy;

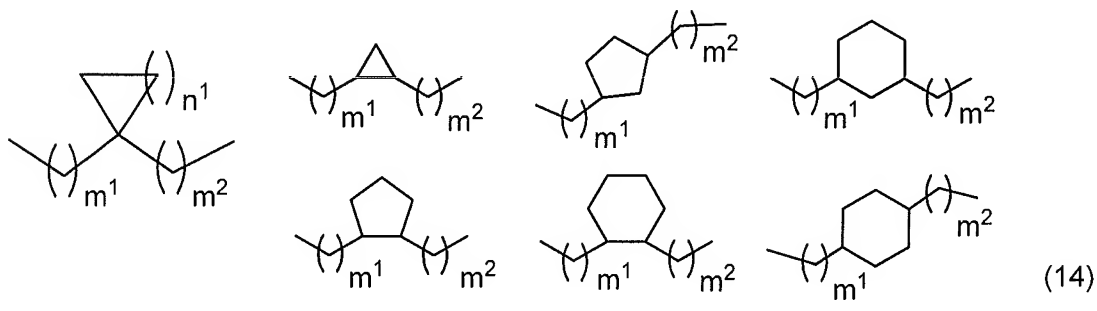
the optionally substituted thiol is thiol, an alkylthio, an aralkylthio, an arylthio, or a heteroarylthio, wherein the alkylthio is methylthio, ethylthio, 2-propylthio, or cyclopentylthio, the aralkylthio is a phenyl-(C<sub>1</sub>-C<sub>8</sub> alkyl)thio, the arylthio is phenylthio or 1-naphthylthio, and the heteroarylthio is pyridylthio or imidazolylthio;

the alkylsulfonyl is a straight chain or branched chain C<sub>1</sub>-C<sub>8</sub> alkylsulfonyl;

the carbamoyl group optionally substituted by an alkyl is carbamoyl, a straight chain or branched chain C<sub>1</sub>-C<sub>6</sub> monoalkylaminocarbonyl, or a straight chain or branched chain C<sub>2</sub>-C<sub>12</sub> dialkylaminocarbonyl;

the lower alkenylene is a C<sub>2</sub>-C<sub>8</sub> alkenylene;

the lower alkylene of the optionally substituted lower alkylene is a straight chain C<sub>1</sub>-C<sub>10</sub> alkylene or an alkylene of the following formulae (14):



wherein  $m^1$ ,  $m^2$  are integer of 0 to 2, and  $n^1$  is an integer of 1 to 4, and the substituent of the optionally substituted lower alkylene is a member selected from an optionally substituted alkyl,

an optionally substituted aryl, an optionally substituted heteroaryl, a halogen atom, an optionally substituted amino, an optionally substituted acyl, an optionally substituted thiol, an optionally substituted hydroxy, and an oxo;

the alkyl of the optionally substituted alkyl is a straight chain or branched chain  $C_1-C_8$  alkyl, or a  $C_1-C_8$  alkyl having a cyclic structure;

the aryl of the optionally substituted aryl is phenyl, 1-naphthyl or 2-naphthyl; and

the substituent of the optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl is a member selected from a halogen atom, a straight chain or branched chain  $C_1-C_3$  alkoxy, a straight chain or branched chain  $C_1-C_3$  alkyl, trifluoromethyl, and trifluoromethoxy.

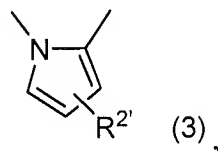
19. (New) The heteroaryl derivative according to claim 18, wherein  $W^3$  is a  $C_2-C_5$  alkenylene, or a pharmaceutically acceptable salt thereof.

20. (New) The heteroaryl derivative according to claim 18 or 19, wherein  $W^1$  and  $W^2$  are an optionally substituted straight chain  $C_1-C_3$  alkenylene, or an optionally substituted  $C_3-C_6$  alkenylene containing a cyclic structure, or a pharmaceutically acceptable salt thereof.

21. (New) The heteroaryl derivative according to claim 18 or 19, wherein  $W^1$  and  $W^2$  are an optionally substituted methylene or ethylene,  $W^3$  is a  $C_3-C_4$  alkenylene, or a pharmaceutically acceptable salt thereof.

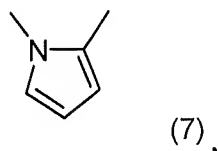
22. (New) The heteroaryl derivative according to claim 18, wherein  $Ar^1$  is an optionally substituted phenylene, and the binding position of  $W^2$  is at meta-position or para-position with respect to the binding position of  $W^3$ , or a pharmaceutically acceptable salt thereof.

23. (New) The heteroaryl derivative according to claim 18, wherein Ring Z is a group of the formula (3):



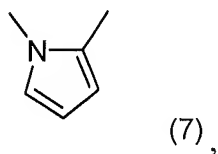
in which the number of  $R^{2'}$  may be one or more, and each is independently selected from a hydrogen atom, methyl, an optionally substituted phenyl, and an optionally substituted heteroaryl,  $W^1$  and  $W^2$  are an optionally substituted methylene or ethylene,  $Ar^1$  is an optionally substituted phenylene,  $W^3$  is a  $C_3$ - $C_4$  alkenylene, or a pharmaceutically acceptable salt thereof.

24. (New) The heteroaryl derivative according to claim 18, wherein Ring Z is a group of the formula (7):



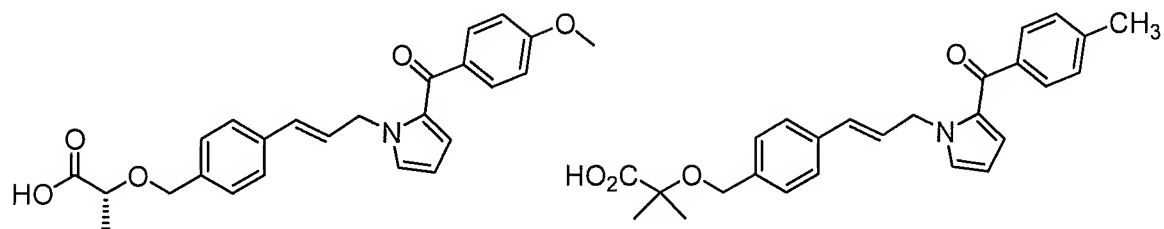
$W^1$  is an optionally substituted methylene,  $W^2$  is methylene,  $Ar^1$  is phenylene,  $W^3$  is propenylene or propylene, or a pharmaceutically acceptable salt thereof.

25. (New) The heteroaryl derivative according to claim 18, wherein Ring Z is a group of the formula (7):



$W^1$  is a methylene optionally substituted by an alkyl having 1 to 3 carbon atoms,  $W^2$  is methylene,  $Ar^1$  is phenylene,  $W^3$  is propenylene or propylene,  $Ar^2$  is a phenyl optionally substituted by an alkyl having 1 to 3 carbon atoms or an alkoxy having 1 to 3 carbon atoms, or a pharmaceutically acceptable salt thereof.

26. (New) The heteroaryl derivative according to claim 18, which is a compound selected from the following formulae (10):



(10)

or a pharmaceutically acceptable salt thereof.